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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/235,986	01/22/99	HENDRICKSON	W 58323/JFW/PT

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EXAMINER

LUNDGREN, J

ART UNIT

1653

PAPER NUMBER

5

DATE MAILED: 10/06/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
09/235,986

Applicant
Hendrickson et al.

Examiner
Jeffrey S. Lundgren

Group Art Unit
1653



☒ Responsive to communication(s) filed on Jun 29, 1999

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire three month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-12 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-12 is/are rejected.

☐ Claim(s) _____ is/are objected to:

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Art Unit: 1653

DETAILED ACTION

Oath/Declaration

1. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

- a. original signatures are missing

Specification

2. The abstract of the disclosure is objected to because of the length in excess of 250 words. Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Art Unit: 1653

Claims 1 and 7 are drawn to a system and method, respectively, with the limitation of pan-genomic determination, wherein "all known structural information" is utilized. Applicants use of the term "all known structural information" is unclear since it impossible to anticipate what structural parameters would be relevant in any one case of practicing the claimed invention. All dependent claims are rejected on the aforementioned grounds.

5. Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 7 are drawn to a system and method, respectively, with the limitation of pan-genomic determination, wherein an ensemble of all known structures is utilized to "further advance an effectiveness of said bioinformatics". All dependent claims are rejected on the aforementioned grounds.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Art Unit: 1653

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cohen et al. (U.S. Patent No. 5,878,373, March 2, 1999).

Cohen et al., disclose a system and a method for predicting the protein fold of a target amino acid sequence (where the experimental 3D structure is undetermined) with a catalogued protein structure. The target sequence is represented by both positional strings and tertiary attributes (residue variability types; see *Summary of the Invention*). The target (or query) is compared against the 3D structures of the "known" structures available in a database by using a dynamic programming procedure to calculate a best fit score indicating the outcome of alignment. By implementing residue variability parameters (parameter that consider hydrophilicity/phobicity), the inventive method has extended capabilities over conventional alignment strategies that identify structural similarities between proteins. The structural properties of the proteins could be compared between proteins classified in the same family

Art Unit: 1653

(although family classification is subjective) or between proteins that typically lack a common grouping. This invention meets the limitations of Applicant's system/method of pan-geneomic determination of three-dimensional structures comprising a database that systematically organizes all known structural information into a geneomic database, and uses the "functional information" to cluster a plurality of known gene products. It is inherent in the cited art that the most closely related matches of multiple known structures to the unknown structure, would often be of the same family themselves. Thus, any number of "functional parameters" could be used in an appropriate algorithm to compare structures within the same database for familial classification or a particular grouping that is in actuality user-defined.

Cohen et al., do not disclose a system/method for 1) protein synthesis; 2) protein screening; 3) protein processing; 4) crystallization; and 5) x-ray crystallography.

Systems for the means of: 1) protein synthesis; 2) protein screening; 3) protein processing; 4) crystallization; and 5) x-ray crystallography, are all well-established in the art as cited by Applicant in the specification of the current application

From the teaching of the references on methods and systems for predicting/comparing the 3D structure of a query sequence (or as a means of classification), from the association of said query primary sequences with sequences of known 3D structure, it is obvious that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. One of ordinary skill in the art would have been motivated to combine the teachings of Cohen et al., with any well-established systems/methods to produce a

Art Unit: 1653

method/system which applies sequence position *and* tertiary characteristics to both the known and unknown 3D sequences as a means for determining the unknown 3D sequence with alignment algorithms, and for family classifications, with the improvement of the said well-established system/method. The systems/methods for the means of: 1) protein synthesis; 2) protein screening; 3) protein processing; 4) crystallization; and 5) x-ray crystallography, are all well-established in the art as cited by Applicant in the specification of the current application. The linking or association of multiple, well-known inventions into a single invention does not necessarily merit a patent, however, unexpected results from the combination of well-known inventions can lend patentable weight to an application. Therefore, these claims are an obvious variant of Cohen et al. Applicant has not shown any evidence in the data presented in the specification which represents a non-obvious or unexpected practical advantage of the claimed invention over the prior art. If Applicant believes that there are unexpected results due to the precise combination of the systems/methods as claimed, Applicant is invited to point specifically to the specification (i.e., page and line numbers) and cite the unexpected improvement over the art. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

8. Claims 1-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eisenberg et al., (U.S. Patent No. 5,436,850, July 25, 1995) in view of Kreisberg et al. (Protein Science, 4, pp. 2405-2410, 1995).

Art Unit: 1653

Eisenberg et al., disclose a computer assisted method for identifying protein sequences that fold into a known three-dimensional structure through attacking the "inverse protein folding" problem. The method compares the amino acid sequences of a known three-dimensional structure to the amino acid sequence of unknown three-dimensional structure. Specifically, the invention of Eisenberg et al., provides a method for relating one-dimensional query sequences directly to known 3D structures which utilize information as it pertains to particular structural characteristics (see column 3, line 61 through column 4, line 52). The structural characteristics considered by Eisenberg et al., include: 1) the accessibility of residues to solvent; 2) polarity of residues; and 3) the local secondary structure. Eisenberg et al., also teach a "Z score", which is the number of standard deviations that for a "best fit" alignment score of the known sequence is above the mean alignment score for other known sequences of similar length. These characteristics are represented by an environmental string of data so that a "best fit" alignment score (S_{ij} ; from the dynamic programming algorithm) between known 3D sequences can be compared to the 1D structure of the query sequence. In other words, Eisenberg et al., utilize a method which brings into consideration both sequence position and tertiary characteristics of known 3D sequence, however, only information pertaining to the primary structure of the sequence which the 3D structure is unknown is utilized in the alignment algorithms.

Eisenberg et al., do not teach the advantages of using secondary or tertiary characteristics (assigned or derived) for the amino acids or amino acid sequence of the query.

Art Unit: 1653

Kreisberg et al., teach a method that is an improvement upon a method of aligning a primary structure of a protein (query) to a protein of a known 3D structure. The improvement comprises imposing secondary structural aspects upon the query sequence as a means to assist alignment for structure predictions. Kreisberg et al. state (page 2406, beginning of second full paragraph):

"For proteins of unknown architecture, knowing which cysteine pairs are disulfide bonded in primary sequences containing more than two cysteines can facilitate the prediction of tertiary structure."

The improvements of this method are demonstrated on page 2407, sixth full paragraph, where the field of the search was reduced considerably through associating conserved cysteines between the query sequence and the known 3D structures. Furthermore, Kreisberg et al., suggest that any constraint (i.e., solvent accessibility, hydrophobic moments), including disulfide bridges, may be useful for assisting the 3D structures in queries (page 2409, first full paragraph).

Moreover, Kreisberg et al., not only teach a method for aligning an unknown sequence to a known sequence in a given database, but disclose a method for drawing structural relationships between protein families (page 2407, starting with the second full paragraph). Kreisberg et al., further describe a method that compares sequences with varying degrees of homology within a protein family, and illustrate how a more comprehensive database with respect to the method of classification (i.e., mutations and/or conserved cysteine data) is advantageous in determining unknown sequence relationships/structures.

Art Unit: 1653

From the teachings of the combined references on methods and systems for predicting/comparing the 3D structure of a query sequence (or as a means of classification), from the association of said query primary sequences with sequences of known 3D structure, it is obvious that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. One of ordinary skill in the art would have been motivated to combine the teachings of Eisenberg et al., with the teachings of Kreisberg et al., to produce a method which applies sequence position *and* tertiary characteristics to both the known and unknown 3D sequences as a means for determining the unknown 3D sequence with alignment algorithms, and for family classifications. Additionally, systems for the means of: 1) protein synthesis; 2) protein screening; 3) protein processing; 4) crystallization; and 5) x-ray crystallography, are all well-established in the art as cited by Applicant in the specification of the current application. The linking or association of multiple, well-known inventions into a single invention does not necessarily merit a patent, however, unexpected results from the combination of well-known inventions can lend patentible weight to an application. Therefore, these claims are an obvious variant of Cohen et al. Applicant has not shown any evidence in the data presented in the specification which represents a non-obvious or unexpected practical advantage of the claimed invention over the prior art. If Applicant believes that there are unexpected results due to the precise combination of the systems/methods as claimed, Applicant is invited to point specifically to the specification (i.e., page and line numbers) and cite the unexpected

Art Unit: 1653

improvement over the art. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

9. No claims are allowable.

10. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Jeffrey S. Lundgren whose telephone number is (703) 306-3221. The Examiner can normally be reached on Monday-Friday from 8:00 AM to 4:30 PM (EST).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Bradley Sisson, can be reached at (703) 308-3978.

Any inquiries of a general nature relating to this application should be directed to the Group Receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted by facsimile transmission. Papers should be faxed to Group 1653 via the PTO Fax Center using (703) 305-3014 or 305-4227. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989.)

Application/Control Number: 09/235,986

Page 11

Art Unit: 1653

JS 9/30/99

Jeffrey S. Lundgren, Ph.D.

Eggerton Campbell

**EGGERTON A. CAMPBELL
PRIMARY EXAMINER**